Title: Overview Review of Monkey Pox Virus

Authors:

1. **Aftab Ahmad**

   Email: aftabahmad927251@gmail.com

   Affiliation: Capital University of science and technology Islamabad Pakistan

2. **Muqaddas Zafar**

   Email: muqqadasszafar666@gmail.com

   Affiliation: Capital University of science and technology Islamabad Pakistan

3. **Rida Zafar:**

   Email: rida22feb2002@gmail.com

   Affiliation: Capital University of science and technology Islamabad Pakistan

4. **Aisha Zulfiqar**

   Email: aisha193004@gmail.com

   Affiliation: Capital University of science and technology Islamabad Pakistan

5. **Urooj Nazir**

   Email: uroojnazir1@gmail.com

   Affiliation: Capital University of science and technology Islamabad Pakistan

Table of Contents

Abstract:

Monkeypox is a zoonotic disease and endemic to western and central Africa, and was first discovered in 1958 and in 1970 when a 3-year-old child from the Equateur region of the Democratic Republic of Congo formed a clinical syndrome similar to smallpox in the region where the smallpox virus had already been interrupted. The cases increased up to 72 in early 2000s. DRC Ministry of Health gathered the data from 2010-2014 and came to the conclusion that the reported cases were exceeding 2000 cases annually. This virus has similar genetic makeup and pathophysiology to smallpox virus with the exclusion that this virus enters from the wildlife source by the means of small lesions on the skin or oral mucous membrane. There is still no proper treatment specifically against monkeypox infections however, monkeypox and smallpox share same genetic material so the antiviral drugs and vaccines developed to protect against smallpox can also be used to treat monkeypox infections. In this article we discussed the emergence, history, mode of infection and vaccines available for the virus. We also gave an insight on the pathophysiology of the virus.

Keywords: Monkeypox virus, Monkeypox; MPV, MPX

Introduction:

Monkey pox virus is a pathogenic virus that belongs to genus orthropoxvirus with a brick shape, enveloped virus 200 _250 nm and replicates in cytoplasm. It has 2 strains WA and CB; WA is less transmissible than CB. Monkeypox disease is zoonotic disease and endemic to western and central Africa. MPV cause infection in human leading to illness similar to small pox categorized by Rash, fever, lesion and Lymphadenopathy (swelling of lymph node). Lesions eventually change their form and develop into papules, vesicles, pustules and lastly crusts. Death rate in unvaccinated people is higher than vaccinated people, 11% fetal outcome.MPV transmit through respiratory droplets and direct contact with fluids secreted from lesion. Bite or scratch also serve as direct source of transfer of MPV. Currently there are no medicines\drugs certified for treatment of infection, although smallpox vaccine provide immunity and is used in limited quantity due to safety concerns. Consequently, MPV spread is prevented by reducing of completely diminishing the physical contact with

infected people, wild animals. Earlier studies have provided evidences of most human-to-humantransmission of MPV within both families and health services; though diminutive data suggested the specific transfer that is involved in spread of MPV. Evidences from previous studies pointed small mammals as reservoirs of MPV although; ultimate definitive animal reservoir is still unknown. Although neutralizing Orthopoxvirus antibodies have been found in a variety of animals, live MPXV has only been obtained from sylvatic animals, from squirrel (Funisciurus sp.) and mangabey (Cercocebusatys).When compared to prior years, the number of MPXV cases in 2013 increased by nearly 600%. During this outbreak, there were several transmission incidents within households, with a median within-household attack rate of 50%. Small mammals were examined for signs of current and previous

History:

It was first discovered in 1958 and in 1970 MPV is declared as human zoonosis when this virus infects 9 months old baby in democratic republic of Congo. An exceptionally large outbreak MPX was recorded, and reported cases persisted over 1997, with highest occurrence rate in August of 1996, March of 1997, and August of 1997. Initial outcomes from 1997 field research point to a new epidemiological pattern in which the maximum numbers of cases are caused by human-to-human spread and the disease is clinically milder. The samples of MPV was initially collected from sick animals in a group of smallpox vaccine proved defensive against severe human MPX infection, which added to the knowledge of the likely zoonotic source **(Nolen, L. D. *et al*, 2015)**.

Size of monkeypox virus is 200X250nm and rectangular shape supported by mammalian cells. Recognition of MPV has taken fourteen years and non-human primates provide a suitable model to study characteristics of Monkeypox infection and related immunological responses occurring in infection. Monkeypox disease is closely related to smallpox disease. Similarity between these two diseases is confirmed by clinical features such as formation of lesions. Monkeypox virus (MPV) has been natural infection from variola virus in humans. This discovery of pox related disease in monkeys has triggered queries concerning epidemiological and clinical relation between these two diseases (Cho, C. T., &Wenner, H. A., 1973).

monkeypox, the infection was not deemed a threat as far as smallpox vaccination was persistent, and a solid commitment to the global eradication of smallpox was made. After that, it had been eradicated from Europe, North America, Eastern Asia, and other hosts other than humans. In equator region of democratic Region of republic of Congo, a child developed small pox like diseases in 1970 and total 59 cases of monkeypox disease were reported from the same area between time span of 1970 to 1980. 47 cases of human MPV were reported in tropical rain forest of Democratic Republic of Congo at the end of 1979, 4 of these 47 were with scars, 23 patients were infected due to person -person transmission and 4 cases occur due to contact with unvaccinated people (Heymann, D. L., 1998).MPX outbreak in USA was reported in 2003 after shipping of mammals (Prairie dogs) from Ghana to Texas. These mammals were infected with MPV and sold to suppliers where these were kept with American native prairie dogs. 20% increase in infected cases was seen by conducting the study in which the active surveillance data of 1980 form health zone and data of 2006-2007 from health zone was compared; this study was conducted in 2010.In 2016 outbreak of MPV occurs in CAR with 26 reported cases and 2 deaths between September–October. Highest case fertility rate was observed during year 1981 to 1985. In 2013 seven human- human transmission actions were suspected and resulting 42 cases were reported (Katy, B. & Peter, L., 2016).

Monkeypox emergence:

The first case in year, a child from the Equateur region of the Democratic Republic of Congo formed a clinical syndrome similar to smallpox in the region where the smallpox virus had already been interrupted. The illness was caused by monkeypox, according to the WHO Collaborating Centers on Smallpox, and another Poxvirus epidemic in Atlanta and Moscow (Heymann, D. L., 1998). The reported outbreaks and confirmed cases are discussed below in Table 1(Reynolds, M.G. & Damon, I. K., 2012)

Human monkeypox in the period 1970-1980:

It was first seen in 1958 in laboratories testing on monkeys, and it later revealed marks of monkeypox infections in several African rodents by testing the blood of animals from Africa. In 1970, the first case of monkeypox in humans was reported when the virus was first discovered in a person

living in distant parts of Africa. Amid the years 1970 to 1980, a total of 59 cases of human monkeypox were detected in Cameroon, Cote d'Ivoire, Liberia, Nigeria, Sierra Leone, and the Democratic Republic of Congo. The Democratic Republic of the Congo's tropical rainforest was the site of all 47 instances documented up to the end of 1979, and 4 (9 percent) of those cases included people who had had a smallpox vaccination. Out of 47 cases, 23 were in serious condition and 8(17%) of the disease were lethal. In certain cases, cases arose in clusters. And the rate of person-to-person transmission (secondary) recorded was 4 out of 47 (9%) while no proposal of tertiary growth was seen. Among the 123 non-vaccinated contacts 4 were considered secondary cases where the rate was 3.3% and among 40 very familiar family members and 3 of them with a secondary attack rate of 7.5 % (LeeLigon, B., 2004). Other 69 cases were reported between 1970 and 1980. One of the reviews also reported the same 59 cases but no reference was given (Rans, N. S., 2018).

The observation in the Democratic Republic of the Congo, 1981-1986:

WHO meeting calculated 100 cases, another report verified 132 reports in1981-1983. Between 1980 and 1986, a number of 350 and 346 cases were reported. Another total of 338 was confirmed by the WHO surveillance program between 1981 and 1986 and 33 deaths were recorded due to the monkeypox virus. Since there was no significant increase in the number of cases arriving from regions not under WHO observation, the rise in MPX cases between 1981 and 1986 was likely the result of strengthened surveillance. The total number of verified MPX cases reported per nation from 1970 through the end of 1986 was 404, despite the fact that the number of yearly reported cases in various countries differs between sources. During the WHO monitoring period (1981–1986) alone, some sources documented 404 cases (Rans, N. S., 2018).

Country	Year	Number of cases	Deaths
Congo Basin			
DRC	1970–present	Cases not fully enumerated[a]	Deaths not fully enumerated[a]
Cameroon	1979/1989	3	0
Central African Republic	1983	6	0
Gabon	1987	2	2
Republic of the Congo	2003	11	1
West Africa			
Liberia	1970	4	0
Sierra Leone	1970	1	0
Nigeria	1971/1978	3	0
Cote d'Ivoire	1971/1981	2	0
Other			
United States (ex. Ghana[b])	2003	47	0
Sudan	2005	10	0

Figure 1: Human monkeypox virus reported from 1970 to 2005*(Reynolds, M.G. & Damon, I. K., 2012)*

Monkeypox outbreak in 1996-1999:

Up until 1996, when Medecins Sans Frontiers (MSF) alerted WHO of a potential monkeypox epidemic in a community residing in KatakoKombe, Sankuru sub-region, Kasai Oriental, no new cases of human monkeypox had been reported to WHO after 1992. A 35-year-old man who feels unwell in the middle of February 1996 was the outbreak's first recorded case. The WHO Collaborating Centre for Smallpox and other Poxvirus Infections at the Centers for Disease Control and Preventions in Atlanta, USA performed a retro-specific investigation that recognized 71 assumed sample-based either on an origin of illness or the occurrence of pockmarks, out of which 6 about 8.5% were lethal, and 11 active cases that were all affirmed as monkeypox in 13 villages (Katako-Kombe health zone, Sankuru Sub-region, Kasai Oriental Region) until 30 (Heymann, D. L., 1998). Between February 1996 and October 1997, 54 communities in the Katako-Kombe health zone and 24 in the Lodia health zone reported a total of 511 suspected cases (Rans, N. S., 2018).

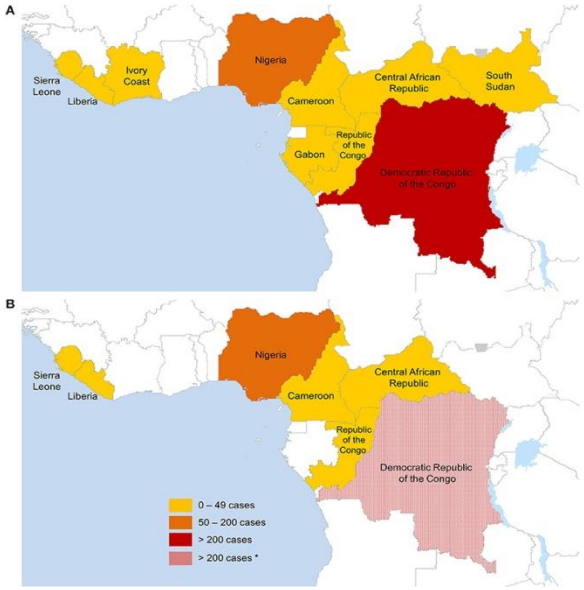

Figure 2: Countries reporting verified cases of monkeypox in people between January 2017 and May 2018 (B) and August 1970 and May 2018 (574 months), respectively (17 months). There were only official sources of data present. data granularity for some outbreaks is lacking (Rans, N. S., 2018).

2000-2009:

A 3-year-old toddler who was sent to the hospital in central Wisconsin with cellulitis and temperature following a prairie dog bite on May 13 was discovered to have a strange illness on May 24, 2003, according to the Wisconsin Division of Public Health (DPH). But on June 2, 2003, two weeks later, proof of a far larger scenario started to surface. The Marshfield Laboratory informed the Wisconsin DPH on that day the mother of the initial case had become unwell on May 26. A sizeable epidemic of monkeypox had

been recorded in Wisconsin, Illinois, and Indiana by July 2003, with 72 confirmed or suspected cases Through May 29 and June 9, 2003, there were 783 cases at the height of the epidemic, and 1026 cases were reported in 2004(LeeLigon, B., 2004). 10 confirmed, 9 probable, and 30 suspected MPX cases were reported between September and December 2005 from 5 villages in Unity State, Sudan 2 in Bentiu, 3 in Modin, 5 in Nuria, 5 in Rubkona, and 4 in Wang Kay) (an area that is now part of South Sudan) (Rans, N. S., 2018).

2010-2018:

In 2010, 10 more cases were seen after the epidemic in the ROC (Likouala region) (2 confirmed, 8 suspected). After the interethnic conflict in the northwest of the DRC, it was believed that this pandemic was related to the influx of DRC migrant's crossways the Ubangi River into the ROC (Democratic Republic of Congo. The viral isolate (81137 nucleotide segment, from E9L to A24R) was sequenced, and phylogenetic analysis showed that it (99.5 percent) most clearly aligned with the virus isolated from the endemic in the ROC in 2003, whereas the virus from the DRC in 1979 and 1996 was less related. In that year (2010), some other cases of MPX were stable in the CAR (Cordillera Administrative Region). After shooting and feeding on a wild rodent (bemba) this disease took place. Additionally, the isolated strain shared a lot of similarities with the strain linked to the endemic in 2001laterally the border between the CAR and the DRC. DRC Ministry of Health gathered the data from 2010-2014 and came to the conclusion that the reported cases were exceeding 2000 cases annually. There wasno less than one assumed case that was informed from every area of the DRC while the biggest number of reports were seen in Equateur and Kasai Orientale provinces (1166 and 708, respectively In 2014, 423 instances were included in the samples, which were drawn from the suspected cases reported from various regions. The findings confirmed that 15 percent (63 samples) of the samples were positive for VZV, 22 percent (92 samples) were negative for both viruses, and 62 percent (264 samples) of the samples were positive for orthopoxvirus. Between 2011 and August 2014, MPX cases were suspected in 4 cases in the North's wooded regions. Through the DRCs passive surveillance program, 587 probable MPX cases between September 2014 and February 2016 were recorded. The province

of Tshuapa and Equateur together accounted for 363 of the recorded cases (135 cases) ROC's Likouala province reported an outbreak of monkeypox that resulted in 88 cases, 7 of which were laboratory-verified and 6 of which resulted in deaths (CFR 6.8 percent). In 2017 of January and August, ROC's Likouala province reported an eruption of monkeypox that resulted in 88 cases, 7 of which were laboratory-verified and 6 of which resulted in deaths (CFR 6.8 percent) (Rans, N. S., 2018).

2019-2022:

During the past few years, the virus has once more spread, this time to many nations across virtually an entire continent. Although the virus spread to endemic nations, no confirmed cases of infection have been reported as of yet. As of May 21, at 13:00, Three WHO areas have reported 92 laboratory-confirmed cases and 28 suspected cases with continuing investigations (Australia, North America, and Europe). No fatalities have been recorded. On May 6, 2022, a UK citizen with a travel history to Nigeria was identified as the index case of the ongoing monkeypox epidemic in 2022.MPXV isolates transported into the United Kingdom in 2018-2019 are biologically tied to the Nigerian MPXV genome, according to the sequencing of the original isolate from the patient in Portugal, acquired on May 4, 2022. The Democratic Republic of the Congo led all endemic countries with 1315 cases of monkeypox between 15 December 2021 and 1 May 2022, followed by Nigeria with 46 cases between 1 January and 30 April 2022, Between 15 December 2021 and 22 February 2022, there were 26 instances in Cameroon, while there were 6 cases in the Central African Republic from March 4 to March 10, 2022. Between 1 January and 8 May 2022, Nigeria reported 111 possible cases of MPXV to the WHO Regional Office for Africa. MPXV is characterized by a sudden onset of temperature and a vesiculo-pustular rash that mostly affects the face, palms, and sole (Thirumalaisamy, V. & Christian, M., 2022).

PATHOGENESIS:

Monkeypox Inhibitor of Complement Enzymes expresses virulence factor as its regulatory function were compared to variola (SPICE) and vaccinia homologous complement regulatory proteins (VCP). As disulfide-linked homodimers composed of 5–30% of MOPICE, SPICE, and VCP in different expression systems.VCP dimers were located in vaccinia virus-infected

mammalian cells. SPICE and VCP's human C3b/C4b terminal is bound by MOPICE as it possesses cofactor activity that is comparable to VCP, although both were 100 times less effective than SPICE. C3 and C5 are convertases of disease accelerating reactivity in SPICE and VCP. All three inhibitors might attach to heparin.

ANTIGENS OF MONKEYPOX VIRUS:

- **MPXV A35R Protein:**

This protein is homolog of A33R protein of Vaccinia virus. As A33R protein requires viral particle transmission from cell to cell. It might be used for diagnostic testing, along vaccination and durg development.

- **MPXV A29 protein:**

This protein is homolog of Vaccinia virus A27 protein having several functions:

1) Heparin binds on cell surface to mediate cell fusion.

2) IMV trafficking on microtubules and IEV formation is required.

3) Integrate A26 protein into viral particles that are developed.

4) Key target for neutralising antibodies.

- **MPXV L1R Protein:**

This protein is homolog of J1R protein of Vaccinia virus it's involved in variety of processes viral development, plaque formation, and virion morphogenesis, it plays a critical role(Lewis-Jones, 2004).

POXVIRUS REPLICATION CELLULAR TROPISM:

The genomes of most block framed Virions range from 130 to 300 kb, and they for every circumstance duplicate in the cytoplasm or adulterated cells. There are eight uncommon chordopoxvirinae genera that dirty people (orthopoxviruses, parapoxviruses, molluscipoxviruses, and yatapoxviruses). Messes have countless outcomes, going from illness with a high ruin rate to poxvirus transmission of contaminations that are safeguarded concerning shape and content. Since individuals from different poxvirus genera appear, apparently, to be same. The straight twofold abandoned DNA genomes of poxvirus family show attributes along these lines, similar to terminal turned base directions and helical pieces with many thickly stuffed open sorting out edges, including something like 90 are basic for poxvirus support. There are various varieties in morphogenesis and replication-related adaptable progress among two or three

poxvirus genera(Frey, 2004). Considering interesting presentation of s non-coordinated genomes, poxvirus has its own host reach, immunomodulation, and pathogenesis. Express quality framework is utilized to dismantle poxvirus attributes since they influence danger of sickness in a dirtied have in any case are outrageous for defilement replication in tissue-culture cells. As destruction of peril qualities conveys the sickness unequipped for imitating in a subgroup of cell social orders that are regularly lenient untamed. The poxvirus duplication cycle incorporates complex series of cytoplasmic exercises, beginning with viral relationship with cell layer and consolidating of microorganism and human cell films. The intracellular replication illustration of vaccinia pollution is smallpox-obliteration immunizer assortment(Upton, 2003)..

It shows viral iota portion is portrayed by quick cell reactions have protein kinase wellsprings and it impacts coming about replication stages as it is driven by viral replication in human cells recalling Toll like Receptors for this method that forestall poxvirus disease decline TLR transmission his wellspring causes the mix of viral mRNA energetically affected by viral early sponsor. This uncoating stage licenses viral DNA to enter the cytoplasm and go presumably as an arrangement for DNA replication and following surges of temporary and late record. As opposed to early record, which is managed by viral transcriptosome proteins encapsidated inside the middle, by and large captivating and late record stages require joint exertion with have incited record factors that help to advantageously convey two surges of viral quality. Poxviruses express exceptional neuroactive proteins that change both the intracellular and extracellular Poxviruses, in besides to have executing factors, express an arrangement of modulatory proteins that change the intra-and extracellular ecological pieces of the destroyed cell. These polluting encoded proteins with everything looked at balance as a wide assortment of antiviral insurance responses set off by contamination disease, including tremendous factors impacting pathways, for instance, cell destruction, interferon enrollment of the antiviral state, stress-incited hailing wellsprings, MHC-bound antigen show, and foes of pathways. Individual poxviruses encode express host-response factors, which are committed for each poxvirus' ability to answer the different antiviral frameworks totally through searched in the degradation site, what's seriously during the spoiling's

dynamic improvement through various cell types and tissues(McLysaght, 2003)..

RESTRICTION PROCESSES IN POXVIRUS-INFECTED CELLS:

Despite the fact that how we might interpret the fundamental characteristic cycles that adjust administrative variables that can impact whether poxvirus infection is liberal or confined is restricted, we can make a few speculations about infection particles connection and confirmation, which is perceived cells determinants required for poxvirus viral genome to join or present viral protein endocytosis, for example, glycosaminoglycan as poxvirus association and entrance into mammalian cells continues (Gubser, 2004)**.** Despite being limited, poxviruses, for example, the molluscum contagiosum infection, can't be duplicated in culture. Regardless of not being delivered in vitro in one or the other cell however imitating in vertebrates basal keratinocytes, it can associate with and enter non-tolerant human cell societies. Chordopoxviruses, then again, join, enter, and start replication processes even inside non-tolerant bug cells. Because of polluting viral strain and dynamic site, viral particles arrive at cytoplasmic stages for starting quality articulation. At this point, just four elements of inborn exercises have been proposed as key limit focuses(Johnston, 2004)**.** Other control designated spots of this kind are probably going to be found from here on out.

CELL-CYCLE CONTROL:

The occasions that can be controlled in a ruined's cell-cycle state. Poxviruses were accepted to be less S-stage subordinate than different various infections, yet there is check displaying their ability to MITOGENICALLY STIMULATE quiet cells basically further creates viral duplication levels(Vanderplasschen, 1998). Poxviruses have been displayed to straightforwardly disturb the limit of express cell-cycle parts in ruined cells, yet whether there is a cozy relationship with cell tropism is as of now dim. Microarray information from HeLa cells treated utilizing vaccinia tainting strain WR show that, but most of cell qualities are controlled, a little division 3 percent are stunningly requested. It would be dazzling to offset affected attributes with quality verbalization plans tracked down in close to sicknesses with have limited illness assortments however the main information open so far is for inactivated changed vaccinia pollution Ankara which stimulates

the understanding of substantially more cell qualities than the WR strain (Locker, 2000).

CELL LINEAGE AND DIFFERENTIATION STATE:

The intracellular process that impact good judgment poxvirus replicative is the dirtied cell's family heritage and package state. Some poxviruses, for example, are subject to the particular section season of the host cell, for instance, the really noted restriction the dynamic replicative molluscum reflecting contamination to keratin got at the epidermal of skin(Blasco, 1993). The telephone parts vital for the ailment to happen with its causing cycle past the hour of early quality verbalization are obfuscated for this ongoing circumstance, however it is through and through critical that the molluscum changing corrupting conveys less immunoregulatory proteins than another human-sullying poxvirus. Different examination have been embraced to concentrate on the constraint of poxvirus-adulterated dendritic cells to convey new antigens considering the significance of dendritic cells for immunogenic responses to poxvirus-based immunizer vectors(Hsiao, 1998). Inquisitively, regardless of what the way that vaccinia contamination is liberal for most sorts of cells, sickness of either evolved or youthful grown-up dendritic cells achieves cut off dirtying resulting to starting quality explanation, showing that these telephones have some particular flaw that makes them impenetrable to strong vaccinia debasement burden(Masters, 2001).

COMPLEMENTING HOST FACTORS:

The intracellular processfor poxvirus replicative coordinates the different executing that ought to appropriate by the infection complete replicative cycle. Other central host unites that are average by poxviruses, similar to the translational equipment in the cytoplasm, are expansive in making mammalian cells, and are not made a point to directly impact tropism(Greber, 2002).. Anyway, the responsiveness of executing record factors from the host cell that is ordinary as parts for moderate and late outstanding record, as VITF-2, might be rate-confining in unambiguous cells. Along these lines, any necessities head cell regulatory pieces of the microtubule-or actin-based motility device would've should destroy overwhelming contamination morphogenesis or flight. Hsp90 Molecular Chaperone is one blueprint of a gender fluid factor that has been shown to straight direct poxvirus

initiating. It necessities to assistant to viral gathering plants and works with the adequacy of vaccinia sickness replication by conveying the with viral focus protein 4a, which would be common for virion gathering(Boehme, 2004).

SIGNAL TRANSDUCTION:

The different sign transduction pathways that direct the brand name cell response to viral corruption are the fourth gathering of intracellular activities that oversee poxvirus replication. The Ifn antiviral state, about which fundamentally all contaminations have made security instruments, is perhaps the most investigated of them. Against interferon methods for poxviruses integrate interferon attestation inhibitors, receptor reflects that block the intervened signal-transduction pathway, and inhibitors of safe suppressants protein go betweens of the antiviral state, including protein kinase is making check that conveyed interferon reactions are basic for staying aware of beyond what many would consider possible against express poxvirus defilements(Bowie, 2002). STAT1-lacking mice can be mortally spoiled with myxoma contamination, but wild-type mice are totally gotten. Besides, in key human fibroblasts, the interferon pathway is an essential restricting piece of myxoma disorder duplication. Not a small bit like the particularly based on interferon system, the cycles by which certain other hailing pathways could impact poxvirus expansion are less evidently known. Different poxviruses, it has truly been found, cover that beginning of positive for ignitable hailing wellsprings, like those induces NF-B through coordinated activities of various hailing inhibitors. Poxviruses encoded substitute apoptosis inhibition is customarily approved during poxvirus sickness. To genuinely spoil mammalian cells, poxviruses ought to manage the mitochondrial farthest reaches of apoptotic motioning, as shown by another enormous audit(Harte, 2003).

POXVIRUS HOST-RANGE GENES:

Examining viral genome replicative relationship with have cells has uncovered understanding into parts of poxvirus tropism. Without a doubt, the key host changes for animal disorders were portrayed in essential work during the 1960s using rabbit pox contamination breaks that failed to duplicate in pig cells. Thusly, the locus that causes this host-range brand name was seen as a viral quality encodes the SERPIN

SPI-1. Anyway, the specific cells focal signs of that fast host range any orthopoxviruses stay dull. The bunny pox contamination SPI-1 protein can bind to it and block CATHEPSIN G, which really is close to in substrate selectivity to a standard serpin. Regardless is that SPI one is most certainly a focal determinantion of poxvirus risk for animal vaccinition fabricates lacking SPI-1 have been shown to be decreased in mice while remaining immunogenic when used as vaccinations. Abutting SPI one different additional poxvirus have range credits are known, much of the time through underhanded infers(Broyles, 1999). For example, consigned recombination crossing out of some pointless poxvirus characteristics drove in prohibitive replication irregularities explicitly cells, and these have been named have range ascribes to highlight this phenotypic imperfection. In a few conditions, have range quality requesting was achieved exclusively following isolating viral quality scratch clones with sheets of regularly sensitive cells. Individual poxviruses have empowered their own certain subgroups of host range as Early examination recommended that particular vaccination sickness separates with casual quality undoing couldn't enable in human cells (Broyles, 1999)Some time later, the K1L, C7L characteristics shown to be head for the completion of the vaccinia corrupting replicative cycle in human cells. Vaccination has been not arranged to complete its replication cycle inside Chinese hamster ovary (CHO) cells considering an intracellular cut off that happens right at season of center quality explanation, not long after viral confining and entry. The K1L/C7L need might be fixed by another cowpox polluting have range quality, CHOhr or CP77, which has really been seen precisely true to form for cowpox replication on CHO cells. Implanting a CHOhr quality in vaccinia or ectromelia debasements licenses them to make in CHO. Besides, so regardless of what the way that progress of changed vaccinia disease that is additionally missing K1L is routinely bound at the early protein mix stage in bunny kidneycells, verbalization of K1L in transfected cells with the K1L quality compensates for the shortfall of the K1L quality and engages improvement of K1L-less vaccinia spoiling through RK13 cells. Both K1L, CHOhr have a spot with the ankyrin-reiterate protein super family, which is known to be vital for protein trades. There is some assertion that influences viral moderate protein understanding capacity at the level the

eukaryotic-translation beginning element 2 K1L has truly been found to frustrate NF-B order in RK13 cells, obviously by decreasing degradation of the inhibitor protein I similarly contains ankyrin goes over. M-Tfive of myxoma debasement, about the really seen poxvirus ankyrin-go over have range protein, is fundamental for ailment replication in hare T cells (Drillien R. S., 2004)**.**This protein viraltruly seen to be crucial myxoma ailment replicative in various changed cells. Again the control of M-T five is dull, but obviously it start and end except for a bunny express modulator, conceivable considering the way that its undisclosed host-cell targets are in general clear across species limits. Starting as of late in the, fair poxviral have range credits with the best impression of the host target are the vaccinia ailment E3L and K3L characteristics, which have been endlessly out examined up for their capacity to hinder have interferon responses. The E3L quality things are two related double stranded RNA proteins cover incitation of central antiviral go betweens, including PKR and OAS while K3L duplicates have work out eIF2 and fills as PKR pseudo-substrate. Likewise, E3L can annihilate type one interferon certification by controlling the approving the interferon conclusive components 3 and 7. Vaccination disease movements lacking E3L are bound in various cells, yet K3L-less vaccinia pollution is just fizzled for youth kidney cells. There is a couple of sign that the specific extents of double stranded RNA ,PKR made debased cells direct the titanic coordinated improvement of E3L and K3L on have cell tropism. The p28-RING zinc protein from ectromelia contamination is dominatingly the depiction of a poxvirus has range protein with a portrayed biochemical cutoff .p28 for destructiveness in mice, and removal of the p28 quality obstructs from reproducing significantly macrophages. The p28 protein capacities as an E3ligaseand the disease's powerlessness to coordinate substrate proteins for individuals influenced and decimation adds to a non-indulgent complete inside corrupted macrophages, yet essential host targets stay (Guerra, 2004).

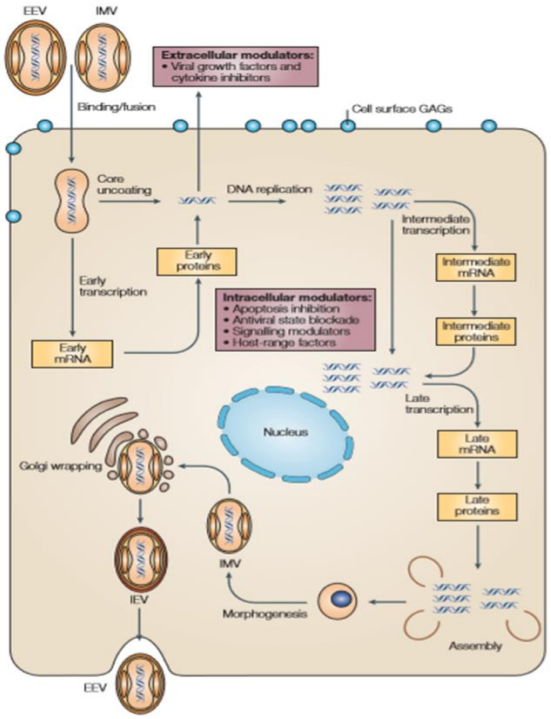

Figure 3: The cycle of poxvirus replication. A complicated but generally similar morphogenic mechanism is used by all poxviruses to reproduce in the cytoplasm of infected cells. Infection can be initiated by two separate infectious viral particles: internal matu

Table 2 | **Host-virus interactions that might regulate poxvirus/cell tropism**

Level of host-virus interactions	Viral factors that require host-cell components	Interacting host-cell factors and pathways
Virus binding and entry		
EEV binding	Unknown	Unknown
IMV binding	VV-A27, D8, H3	Glycosaminoglycans, laminins
Fusion/endocytosis	VV-A28, others?	Host membranes, raft-dependent?
Intracellular events		
Cell-cycle control	Viral growth factors (VGF, vVEGF)	S-phase regulators, p53
Differentiation state	Unknown	Cell lineage factors
Complementing factors		
Core uncoating	Core structural protein(s) (?)	Unknown
Transcription	Viral RNA polymerase complex	Intermediate/late transcription factors
Protein folding	Core protein 4a	Hsp90
Virion trafficking	VV-A36 of IEV	N-WASP, Nck, WIP, Src/Abl-kinases
Signal transduction		
Antiviral state	VV-E3L/K3L, tyrosine phosphatase	Interferon signalling, PKR, STAT
Kinases	Unknown targets	PAK1, ERK1/2
Signalling	VV-KIL, N1L, A52R; MC159L; M150R	NF-κB
Apoptosis	M-T5, M-T2, M-T4, M11L, VV-F1L, SPI-1, SPI-2, EV-p28	Cell death machinery

CEV, cell-associated enveloped virus; EEV, extracellular enveloped virus; ERK1/2, extracellular regulated kinases 1, 2; EV, ectromelia virus; Hsp90, heat shock protein 90; IMV, intracellular mature virus; MC, molluscum contagiosum; M, myxoma; NF-κB, nuclear factor-κB; Nck, Novel cytoplasmic kinase; N-WASP, neuronal Wiskott–Aldrich syndrome protein; PAK1, p21-activated kinase 1; PKR, protein kinase R; SPI, serine proteinase inhibitor; STAT, signal transducer and activator of transcription; VGF, vaccinia growth factor; vVEGF, viral vascular endothelial growth factor; VV, vaccinia virus; WIP, WASP-interacting protein.

Figure 4: Host virus interactions regulating cell tropism

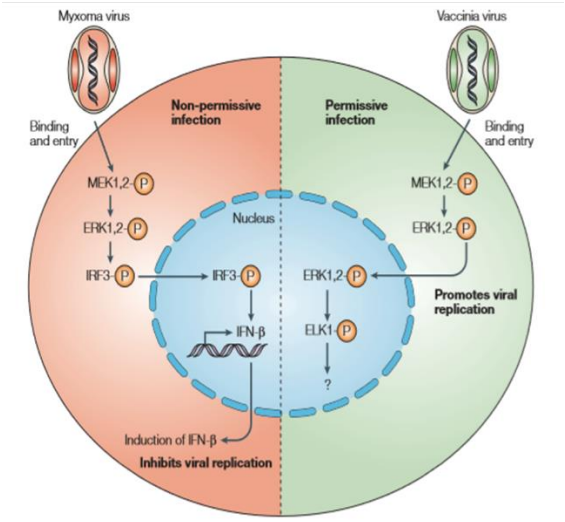

Figure 5: Poxvirus tropism is influenced by intracellular signalling processes. A comparison of the infection of primary murine embryo fibroblasts (pMEFs) by two poxviruses, one of which (myxoma virus) is non-permissive due to an increased type-I interferon resp

Monkeypox pathogenesis and Transmission in Prairie Dogs:

The first human monkeypox case was identified and reported in the United States in May and June 2003. Manyvictims with this feverish cyst rash sickness apparently developed the contamination from prairie dogs which in turn became sick after the interaction with several unusual African rodents (Funiscuirus spp., Heliosciurus spp., Cricetomys spp., Antherurus spp., Graphirurus spp., and Hybomys spp.,)

brought to the United States from Ghana in April 2003. Few African gnawers fell ill during the shipment and expired soon after reaching the United States (Guarner, 2004).

No studies were published regarding the immunohistochemical and histopathogenesis studies of those animals that spontaneously developed the disease. The phenomena of transmission between a diseased animal and a human are still not clear. The tongue and conjunctival lesions of prairie dogs show an abundance of mature poxvirus particles and viral antigens; therefore, the direct interaction with the spittle and exudates from the lesions can greatly transmit the disease to the skin or mucous membrane of different hosts. In the following, the lungs are the suitable site of infection for the rapid multiplication of virus in the bronchi and lung parenchyma which probably caused the infection to spread to other people and rodentsafter the diseased fauna coughed and distributedin factious precipitations. The respiratory path of infection in rodents is also suggested by the pneumonic course in these prairie dogs (Guarner, 2004).

Because they are tiny, widespread, and prone to severe monkeypox viral illness, prairie dogs may provide great animal models for further research into monkeypox infections. In *Cynomolgus* monkeys experimentally exposed to monkeypox virus by inhalation, the clinical characteristics seen in prairie dogs, including necrotizing bronchopneumonia, were seen. The lower respiratory epithelium in these animals served as the virus's major site of reproduction.The virus is delivered to the lymphoid tissues, where it underwent the second viral replication and is seeded in various tissues, counting the skin, mouth mucosa, gastrointestinal tract, and reproductive system tissues. Secondary viral replication sites in this monkey model produced necrotizing lesions. Other species, such as prairie dogs that got sick and perished during the U.S. epidemic, have been observed with necrotizing lesions containing pathological antigens in lymphoid organs. Conjunctivae tongue and bronchi were the main sites of infection by the monkeypox virus. Infested epithelial cells had significant ballooning degeneration and thick, eosinophilic cytoplasmic granules which were hard to identify from keratohyalin bodies histopathologically. For diagnostic reasons, eosinophilic, ground-glass staining in the nuclei of epithelial cells that occasionally merged to form syncytia must be distinguished from herpetic inclusions. In the infected epithelial cells,

the eosinophilic cytoplasmic granules seen have been identified by IHC as viral inclusions, and EM analysis has supported these results. In other cells, such as macrophages and fibroblasts Orthopoxvirus antigens were detected in the prairie dogs that were the subject of the study, particularly in regions close to infected epithelial cells. An identical IHC discoloration outline seen on the tongue and conjunctiva of theinfested prairie dogs was observed in histo-pathologic examinations of skin vesicular lesions on humans. The source of exposure may influence variations in sickness severity, the mode of transfer (such as direct muco-cutaneous contact vs inhalational contact), the quantity of virus injected, the viral strain, or the vulnerability of the patient. The relevance of host susceptibility, including prior immunity, is supported by epidemiologic investigations of human monkeypox infections, which demonstrate that youngsters and people who have not yet received the smallpox vaccine can develop serious illnesses and squeal. This contagion of the virus infection in people and animals serves as an essential reminder to keep a watch on monitoring programs for febrile rash disorders developed to identify possible bioterrorism strikes with the smallpox virus. These tools might be helpful for spotting new infections (Guarner, 2004).

These prairie dogs were examined for monkeypox virus infection using a number of techniques. The virus may be seen in the setting of histology thanks to IHC research. While EM and culture showed viral replication, molecular research was necessary to identify the unique characteristics of the monkeypox virus. Standard PCR and RFLP failed to detect monkeypox DNA in the prairie dogs under study. However, as RT-PCR is more delicate and can precisely titrate up till 4–10 DNA copies, it was able to identify monkeypox viral DNA (Mackay, I. M. $ Arden, K. E., & Nitsche, A., 2002).

TRANSMISSION:

Monkeypox can be sent from one individual to another by direct actual contact, particularly sexual contact. In spite of the fact that it is obscure if monkeypox might be communicated physically (e.g., by sperm or vaginal emissions), direct skin-to-skin contact to wounds during sex acts can disperse the infection. Rashes of monkeypox are sometimes present on the privates and in the mouth, which would be thoroughly considered to elevate to transmission sexual

contact. Where there are skin or mouth sores, mouth-to-skin contact could bring about transmission. Rashes brought about by monkeypox could impersonate those brought about by physically sent diseases like herpes and syphilis. This could make sense of why a significant number of the ongoing flare-up's cases have been distinguished among guys looking for care at sexual wellbeing facilities(Drillien R. S., 2004).

Treatment:

1. Vaccination:

Ankara vaccine:

Ankara vaccine which is licensed by food and Drug administration (FDA) and European Medicine Agency (EMA) is an attenuated third generation modified vaccine which can be effective against Monkeypox virus and smallpox virus. This vaccine is being used for adults (18 years or older) who are at higher risk of smallpox and monkeypox (Alakunle, E., 2020).

Ankara vaccine is defective-replicative vaccine which is recommended by CDC. Vaccination after exposure to virus is significant within four days. Ankara vaccine has two shots which are given a time break of four weeks. Ankara vaccine is live attenuated. It is safe and does not disseminate/spread or create any lesion on skin when compared to vaccinia. It produces antibodies in patient infected with monkeypox virus, especially those which are immunocompromised.

European Commission has authorized marketing for immunization of the general adult population, including those who are immunocompromised, maintained in the United States' Strategic National Stockpile (McCollum, A. M., 2013).

Vaccinia vaccine:

In 2003, during endemic in USA, CDC (center for disease control) suggested smallpox vaccine for the treatment of monkeypox which only reduced the signs of disease but was not able to cure the disease. There is still need for safer second generation vaccinia vaccine, as it is causes health issues such as myocarditis and hiccups in patients who are immunocompromised. Due to its effects on health on people with compromised immunity it is not recommended by CDC and WHO because it caused 268 deaths in Germany. It is not recommended for healthcare workers, investigators, veterinarians, animal worker, military

personnel, and those who are fully exposed to virus

These are licensed vaccination in the United States, currently available to specific populations from the Strategic National Stockpile (McCollum, A. M., 2013).

VIG:

Immune globulin is not recommended for the treatment of smallpox complications by the CDC; rather, it is only advised for preventative use in highly immunocompromised individuals exposed to MPXV. Similar to ST-246, VIG is still classified as an IND (Alakunle, E., 2020).

The effectiveness of monkeypox complications treatment using vaccinia immune globulin (VIG) is not known. Although it is unknown whether VIG is beneficial in this situation, it can be used in severe cases of human monkeypox. When smallpox immunisation is contraindicated for an exposed person with significantly compromised cellular immunity, VIG can be considered as prophylactic (B D Guilo, D., 2004).

2. Medication:

Antivirals:

- **Tecovirimat:**

Tecovirimat (4-trifluoromethylphenol)is approved by FDA and is recommended by CDC. It is also known as TPOXX. It is clinically tested on animal models. It blocks the releases of virus particles from cells in cells infected with virus. There is no evidence of its effectiveness in humans but studies have shown that is it safe to use. It was introduced in 2005. Tecovirimat inhibits the replication of multiple species of orthopoxviruses. In case of bioterrorism, this antiviral has been stocked by US Strategic stockpile to use against smallpox virus (Kabuga, A. I., & elZowalaty, M. E. (2018).

TPOXX interacts with F13L gene which in turn stops the extracellular viruses from further proliferation. TPOXX cytotoxicity in human cell lines is less than 50uM. F13L gene product produces phospholipases, this phospholipase is used by protein complex which is involved in enveloping of mature virus inside the cell. This protein catalyzes the process of formation of envelope (Alakunle, E., 2020).

- **ST-246:**

Cellular release of virus particles can be blocked by using ST-246 drug. It has been observed that this antiviral is effective against the treatment of different species of Orthopoxviruses (McCollum, A. M., & Damon, I. K., 2013).

- **Cidofovir:**

Viral DNA polymerase is involved in replication of viral genome. Cidofovir can inhibit the viral DNA replication by inhibiting the activity of viral DNA polymerase. It is given intravenously while considering hyrdration. Besides it causes neurotoxicity (McCollum, A. M., & Damon, I. K., 2013). This antiviral is used against cytomegalovirus retinitis for patients infected with HIV. It has greater efficacy in immunodefiecent patients who severely infected with molluscum contagiosum virus. It is active when use against poxviruses such as variola, vaccinia, cowpox, and monkeypox (Stittelaar, K. J., 2005).

- **Brincidofovir:**

Brincidofovir or CMX-001 has less neurotoxicity than cidofovir, it is modified cidofovir. Its antiviral activity has been proven effective against species of orthopoxviruses (McCollum, A. M., & Damon, I. K., 2013).

When compared with cidofovir, Brincidofovir is more effective against MPXV, CPXV, and VACV in vitro because of its better antiviral activity and higher cellular toxicity. It also has higher selective index than cidofovir due to its better efficacy against these viruses, its efficacy is 25 times which is higher than cidofovir. Intracellular enzymes convert brincidofovir into active form which also increases its efficacy. Cidofovir gets activated by cellular kinases which add a phosphate group into monophosphate nucleotide analogue of cidofovir which makes its capable of inhibiting viral DNA polymerase. Brincidofovir follows the same path. Brindcidofovir stops the synthesis of viral DNA. Both of these antivirals inhibit the viral DNA polymerase (Alakunle, E., 2020).

Conclusion:

Monkeypox disease is zoonotic disease and endemic to western and central Africa. MPV cause infection in human leading to illness similar to small pox categorized by Rash, fever, lesion and Lymphadenopathy (swelling of lymph node). Death rate in unvaccinated people is higher than vaccinated people, 11% fetal outcome. MPV transmit through respiratory droplets and direct contact with fluids secreted from

lesion. Bite or scratch also serve as direct source of transfer of MPV. Currently there are no medicines\drugs certified for treatment of infection. It was first discovered in 1958 and in 1970 MPV is declared as human zoonosis when this virus infects 9 months old baby in democratic republic of Congo. An exceptionally large outbreak MPX was recorded, and reported cases persisted over 1997, with highest occurrence rate in August of 1996, March of 1997, and August of 1997. MPX outbreak in USA was reported in 2003 after shipping of mammals (Prairie dogs) from Ghana to Texas. These mammals were infected with MPV and sold to suppliers where these were kept with American native prairie dogs. The numerous signal-transduction pathways that coordinate the intrinsic cell responses to the viral infection are the fourth type of intracellular activities that govern poxvirus replication. The interferon-mediated antiviral state, for which virtually all viruses have evolved defense mechanisms, is perhaps the well-studied of them**.** The tongue and conjunctival lesions of prairie dogs show an abundance ofsince these lesions contain viral antigens and mature poxvirus particles, additional hosts' skin or mucous membranes may have come into direct touch with the monkeypox virus through saliva or exudates from these lesions**.** The treatment includes the Ankara vaccine which is licensed by the food and Drug Administration (FDA) and European Medicine Agency (EMA), is an attenuated third-generation modified vaccine that can be effective against Monkeypox virus and smallpox virus. The use of VIG can likely be used in serious cases of human MPXV, but it is still unknown of the benefits it provides in this setting**.**

Abbreviations:

3. MPV
4. MPX
5. WHO
6. MSF
7. FDA
8. VIG
9. DPH
10. CAR
11. DRC
12. ROC
13. VZV
14. SPICE
15. VCP
16. MOPICE
17. IMV
18. IEV
19. MHC
20. TLR
21. IHC
22. PCR
23. RFLP
24. CDC
25. EMA
26. HIV

References:

- Nolen, L. D., Osadebe, L., Katomba, J., Likofata, J., Mukadi, D., Monroe, B., Doty, J., Kalemba, L., Malekani, J., Kabamba, J., Bomponda, P. L., Lokota, J. I., Balilo, M. P., Likafi, T., Lushima, R. S., Tamfum, J. J., Okitolonda, E. W., McCollum, A. M., & Reynolds, M. G. (2015). Introduction of Monkeypox into a Community and Household: Risk Factors and Zoonotic Reservoirs in the Democratic Republic of the Congo. *The American journal of tropical medicine and hygiene*, *93*(2), 410–415. https://doi.org/10.4269/ajtmh.15-0168
- Cho, C. T., &Wenner, H. A. (1973). Monkeypox virus. *Bacteriological reviews*, *37*(1), 1-18.
- Heymann. D.L, Szczeniowski. M, Esteves. K, (1998). Re-emergence of monkeypox in Africa: a review of the past six years, *British Medical Bulletin*, 54(3), 693–702, https://doi.org/10.1093/oxfordjournals.bmb.a011720
- Brown, Katy & Leggat, Peter. (2016). Human Monkeypox: Current State of Knowledge and Implications for the Future. Tropical Medicine and Infectious Disease. 1. 8. 10.3390/tropicalmed1010008.
- B.LeeLigon. (2004). Monkeypox: A review of the history and emergence in the Western hemisphere. *Seminars in Pediatric Infectious Diseases*,15(4), 280-287.
- https://doi.org/10.1053/j.spid.2004.09.001.
- Rans, N. S. (2018). Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans. *Frontiers in Public Health*, 6(1), 2296-2565. https://www.frontiersin.org/article/10.3389/fpubh.2018.00241
- Mary G. Reynolds, Inger K. Damon. (2012). Outbreaks of human monkeypox after cessation of smallpox vaccination. *Trends in Microbiology*, 20 (2), 80-87. https://doi.org/10.1016/j.tim.2011.12.001
- Velavan, Thirumalaisamy& Meyer, Christian. (2022). Monkeypox 2022 outbreak: An update. Tropical Medicine & International Health. DOI:10.1111/tmi.13785
- Lewis-Jones, S., 2004, A useful summary of the poxviruses that can zoonotically infect man, which indicates which of these infections are clinically important, Zoonotic poxvirus infection in humans, 17, 81–89, Url:https://www.nature.com/articles/nrmicro1099.pdf
- Guarner, J., Johnson, B. J., Paddock, C. D., Shieh, W. J., Goldsmith, C. S., Reynolds, M. G., Damon, I. K., Regnery, R. L., Zaki, S. R., & Veterinary Monkeypox Virus Working

Group (2004). Monkeypox transmission and pathogenesis in prairie dogs. *Emerging infectious diseases*, *10*(3), 426–431.https://doi.org/10.3201/eid1003.030878

- Mackay, I. M., Arden, K. E., &Nitsche, A. (2002). Real-time PCR in virology. *Nucleic acids research*, *30*(6), 1292–1305. https://doi.org/10.1093/nar/30.6.1292

- Frey, S. E. &Belshe, R. B., 2004,Poxvirus zoonosesputting pocks into context. N. Engl. J. Med. 350, 324–327, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Upton, C., Slack, S., Hunter, A. L., Ehlers, A. & Roper, R. L., 2003, Poxvirus orthologous clusters: toward defining the minimum essential poxvirus genome. J. Virol. 77, 7590–7600, Url:https://www.nature.com/articles/nrmicro1099.pdf

- McLysaght, A., Baldi, P. F. &Gaut, B. S., 2003 Extensive gene gain associated with adaptive evoluton of poxviruses. Proc. Natl Acad. Sci. USA 100, 15655–15660, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Gubser, C., Hue, S., Kellam, P. & Smith, G. L., 2004, Poxvirus genomes: a phylogenetic analysis. J. Gen. Virol. 85, 105–117, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Johnston, J. B. & McFadden, G., 2004, Technical knockout: understanding poxvirus pathogenesis by selectively deleting viral immunomodulatory genes. Cell. Microbiol.9, 695–705, Url:https://www.nature.com/articles/nrmicro1099.pdf
- Vanderplasschen, A., Hollinshead, M. & Smith, G. L., 1998, Intracellular and extracellular vacciniavirions enter cells by different mechanisms. J. Gen. Virol. 79, 877–887, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Locker, J. K. et al., 2000, Entry of the two infectious forms of vaccinia virus at the plasma membane is signalingdependent for the IMV but not the EEV. Mol. Biol. Cell11, 2497–2511, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Blasco, R., Sisler, J. R. & Moss, B., 1993, Dissociation of progeny vaccinia virus from the cell membrane is regulated by a viral envelope glycoprotein — effect of a point mutation in the lectin homology domain of the A34R gene. J. Virol. 67, 3319–3325, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Hsiao, J.-C., Chung, C.-S. & Chang, W., 1998, Cell surface proteoglycans are necessary for A27L protein-mediated cell fusion: identification of the N-terminal region of A27L

protein as the glycosaminoglycan-binding domain. J. Virol. 72, 8374–8379, Url:https://www.nature.com/articles/nrmicro1099.pdf

- Masters, J. et al., 2001, Poxvirus infection rapidly activates tyrosine kinase signal transduction. J. Biol. Chem. 276, 48371–48375, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Greber, U. F., 2002, Signaling in viral entry. Cell. Mol. Life Sci. 59, 608–626, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Boehme, K. W. & Compton, T., 2004, Innate sensing of viruses by Toll-like receptors. J. Virol. 78, 7867–7873, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Bowie, A. et al., 2002, A46R and A52R from vaccinia virus are antagonists of host IL-1 and Toll-like receptor signaling. Proc. Natl Acad. Sci. USA 97, 10162–10167, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Harte, M. T. et al., 2003, The poxvirus protein A52R targets Toll-like receptor signaling complexes to suppress host defense. J. Exp. Med. 197, 343–351, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Broyles, S. S., Liu, X., Zhu, M. & Kremer, M., 1999, Transcription factor YY1 is a vaccinia virus late promoter activator. J. Biol. Chem. 274, 35662–35667, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Guerra, S. et al., 2004, Microarray analysis reveals characteristic changes of host cell gene expression in response to attenuated modified vaccinia virus Ankara infection of human HeLa cells. J. Virol. 78, 5820–5834, Url: https://www.nature.com/articles/nrmicro1099.pdf

- Drillien, R., Spehner, D. & Hanau, D., 2004, Modified vaccinia virus Ankara induces moderate activation of human dendritic cells. J. Gen. Virol. 85, 2167–2175, Url: https://www.nature.com/articles/nrmicro1099.pdf
- Alakunle, E., Moens, U., Nchinda, G., & Okeke, M. I. (2020). Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution. *Viruses*, *12*(11), 1257. https://doi.org/10.3390/v12111257

- Stittelaar, K. J. (2005). *Antiviral treatment is more effective than smallpox vaccination upon lethal monkeypox virus infection*. Nature. Retrieved June 22, 2022, from https://www.nature.com/articles/nature04295
- Kabuga, A. I., &elZowalaty, M. E. (2018). A review of the monkeypox virus and a recent outbreak of skin rash disease in Nigeria. *Journal of Medical Virology*, *91*(4), 533–540. https://doi.org/10.1002/jmv.25348
- McCollum, A. M., & Damon, I. K. (2013). *Human Monkeypox*. OUP Academic. Retrieved June 22, 2022, from https://academic.oup.com/cid/article/58/2/260/335791?login=true
- B D Guilo, D., &EckBurg, P. B. (2004). Human monkeypox: an emerging zoonosis. *The Lancet Infectious Disease*, *4*(1), 15–25. https://doi.org/10.1016/S1473-3099(03)00856-9